Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 1-3, 6, 8, 14, 15, 18, 20, 21, 27, 28, 31, 32, 34, 39, 42 and 43 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the Examiner set forth certain allegedly unclear language which appears in the claims.

In response to the rejection of claims 1, 3, 8, 15, 28, 34, 39 and 42, applicants point out that these claims have been canceled, rendering the rejection thereof moot.

In response to the rejection of canceled claims 2, 6, 14, 18, 20, 21, 27, 31, 32 and 43, which applicants understand to apply to new claims 58-68, applicants respectfully traverse. Applicants note that claims 58-68 are clear and definite, in that they do not recite the language objected to by the Examiner.

In view of the above remarks, applicants maintain that new claims 58-68 satisfy the requirements of 35 U.S.C. §112, second paragraph.

Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner also rejected claims 1-3, 6, 8, 14, 15, 18, 20, 21, 27, 28, 31, 32, 34, 38, 39, 42 and 43 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to allow one skilled in the relevant art to which it pertains

to make and/or use the invention commensurate in scope with the claims.

In response to the rejection of claims 1, 3, 8, 15, 28, 34, 39 and 42, applicants note that these claims have been canceled.

In response to the rejection of claims 2, 6, 14, 18, 20, 21, 27, 31, 32, 38 and 43, which applicants understand to apply to new claims 58-68, applicants respectfully traverse.

Briefly, new claims 58-61 provide a method for predicting pregnancy outcome in a subject. Claim 62 provides a method for determining the amount of the early pregnancy-associated molecular isoform of hCG present in a sample. Claims 63-66 provide diagnostic kits for predicting pregnancy outcome. Claim 67 provides an antibody which binds to the early pregnancy-associated molecular isoform of hCG recognized by the antibody B152. Finally, claim 68 provides the isolated early pregnancy-associated isoform of hCG recognized by the B152 antibody.

The Examiner states that the subject application is enabling for methods relying on the B152 antibody, but not for any other antibodies which bind to the analyte detected by B152, i.e., the early pregnancy-associated molecular isoform of hCG.

Applicants understand the Examiner's position to be based upon an assumption that specific knowledge about the epitope recognized by the B152 antibody is required to obtain additional antibodies which bind to the same analyte as B152. Applicants disagree with this assumption. Additional antibodies which bind to the same analyte as the B152 antibody can be identified without undue experimentation, using a

modified competitive binding assay in which B152 is labeled. Such an assay requires only a source of analyte and the B152 antibody itself. Additional antibodies, produced using the analyte as immunogen, are screened for their ability to compete with B152 for binding to the immobilized analyte. The instant specification teaches several sources for the early pregnancy-associated molecular isoform of hCG, including urine from pregnant women and choriocarcinoma cells. Applicants note that a purified source of the analyte is not required, since the control for binding specificity is provided by competition with the B152 antibody.

In view of the teachings of the instant specification and the high level of skill in the art, applicants maintain that no undue experimentation would be required to practice this invention. Therefore, claims 58-68 satisfy the requirements of 35 U.S.C. §112, first paragraph.

Provisional Obviousness-Type Double Patenting Rejection

The Examiner provisionally rejected claims 1-3, 6, 8, 14, 15, 18, 20, 21, 27, 28, 31, 32, 34, 38, 39, 42 and 43 as allegedly unpatentable over claims 53, 59, 60, 65, 71, 72 and 77-82 of copending application U.S. Serial No. 09/017,976 under the judicially created doctrine of obviousness-type double patenting. The Examiner stated that the subject matter claimed in the instant application is fully disclosed in the copending application.

In response to the Examiner's provisional rejection, but without conceding the correctness thereof, applicants will consider filing a terminal disclaimer in the instant application should the provisional rejection be converted to a

non-provisional rejection pursuant to the terms of M.P.E.P. §804.

Rejections Under 35 U.S.C. §103(a)

The Examiner rejected claims 1-3, 8, 14, 15, 27, 28, 31, 34, 38, 39 and 42 under 35 U.S.C. §103(a) as allegedly unpatentable over Penfold et al. (1997) in view of Morton et al. (1988) and further in view of Sueoka et al. (1992).

In response to the Examiner's rejection of claims 1, 3, 8, 15, 39 and 42, applicants note that these claims have been canceled, rendering the rejection thereof moot.

In response to the Examiner's rejection of canceled claims 2, 14, 27, 28, 31, 34 and 38, which applicants understand to apply to new claims 58-67, applicants respectfully traverse.

The instant invention provides methods and reagents for predicting pregnancy outcome. This invention is based upon the *surprising* discovery of a correlation between pregnancy outcome and urinary levels of the early pregnancy-associated molecular isoform of hCG. Methods and reagents are provided for the determination of this analyte in a sample.

To establish a *prima facie* case of obviousness, the Examiner must demonstrate three things with respect to each claim. First, the Examiner must establish that the cited references, when combined, teach or suggest every element of the claim. Second, she must establish that one of ordinary skill would have been motivated to combine the teachings of the cited references at the time of the invention. And third, she must

establish that there would have been a reasonable expectation that the claimed invention would succeed.

Applicants maintain that the cited references fail to support a *prima facie* case of obviousness because they do not teach or suggest each and every element of the claimed invention. That is, the cited references fail to teach or suggest methods for quantitatively determining the early pregnancy-associated molecular isoform of hCG in a sample.

Rather, Penfold teaches a two-site immunoassay for the detection of analytes *generally*, and Morton and Sueoka each describe an "early pregnancy factor" which is unrelated to the analyte of the instant invention.

In support of the distinction between the "early pregnancy factor" taught by Morton and Sueoka and the early pregnancy-associated molecular isoform of hCG, applicants point to Morton, 1998, attached hereto as **Exhibit A**. This reference states that "early pregnancy factor" is a member of the *heat shock family* of chaperone proteins. In contrast, the early pregnancy-associated molecular isoform of hCG belongs to a structurally and functionally distinct protein family, namely the peptide hormones known as gonadotropins.

Thus, the cited references fail to teach at least one element of the claimed methods, namely the quantitative determination of the early pregnancy-associated molecular isoform of hCG. In addition, it follows that the cited references also do not create a motive to combine or a reasonable expectation of success. Accordingly, the Examiner has failed to set forth a *prima facie* case of obviousness over Penfold, Morton and Sueoka.

The Examiner also rejected claims 6, 18, 20, 21 and 32 under 35 U.S.C. §103(a) as allegedly unpatentable over Penfold, Morton and Sueoka, and further in view of Birken et al. (1993).

In response to the Examiner's rejection, which applicants understand to apply to new claims 58-67, applicants respectfully traverse.

The claimed invention, as well as Penfold, Morton and Sueoka, are described above. Birken teaches an analytical method for separating intact hCG from nicked hCG and the hCGβ core fragment using column fractionation.

Birken also teaches antibodies B108 and B109 which recognize intact hCG. Applicants maintain that this reference fails to overcome the deficiency of Penfold, Morton and Sueoka recited above. In particular, Birken does not teach or suggest the early pregnancy associated molecular isoform of hCG, or a method for its quantitation.

For the above reasons, applicants maintain that the Examiner has failed to set forth a *prima facie* case of obviousness over Penfold, Morton, Sueoka and Birken, since these references do not teach all elements of the invention and do not create a motive to combine or a reasonable expectation of success.

In view of the above remarks, applicants maintain that claims 58-67 satisfy the requirements of 35 U.S.C. §103(a).

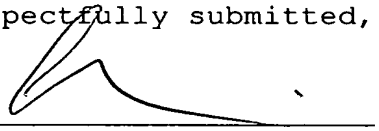
Summary

In view of the remarks made herein, applicants maintain that the claims pending in this application are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, other than the enclosed $55.00 extension fee, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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9/16/02

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1: Immunol Cell Biol 1998 Dec;76(6):483-96

Early pregnancy factor: an extracellular chaperonin 10 homologue.

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Early pregnancy factor (EPF) has been identified as a homologue of chaperonin 10 (cpn10) with immunosuppressive and growth factor properties. As a homologue of cpn10, it belongs to the heat shock family of proteins (hsp) but, unlike other members of this family, EPF is detected extracellularly. Early pregnancy factor was first discovered in pregnancy serum by the rosette inhibition test, and the novelty of its discovery was that its presence could diagnose pregnancy within 6-24 h of a fertile mating. As well as being a monitor of the presence of a viable embryo, it is necessary for embryonic survival. In this capacity it acts as both an immunosuppressant and growth factor. Early pregnancy factor is also a product of proliferating primary and neoplastic cells and functions as an autocrine growth factor both in vivo and in vitro. It has a modifying effect on the outcome of experimental autoimmune encephalomyelitis, an animal model of multiple sclerosis. Early pregnancy factor is considered to be one of the major factors involved in the modification of multiple sclerosis observed during pregnancy.

Publication Types:
Review
Review, Tutorial

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